Complete Summary

GUIDELINE TITLE

Hormone therapy for the prevention of chronic conditions in postmenopausal women: recommendation statement.

BIBLIOGRAPHIC SOURCE(S)

U.S. Preventive Services Task Force. Hormone therapy for the prevention of chronic conditions in postmenopausal women: recommendations from the U.S. Preventive Services Task Force. Ann Intern Med 2005 May 17;142(10):855-60. [30 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This release updates a previously published guideline: Postmenopausal hormone replacement therapy for primary prevention of chronic conditions: recommendations and rationale. Ann Intern Med 2002 Nov 19;137(10):834-9.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Chronic conditions including:

- Osteoporosis and fractures
- Colorectal cancer
- Breast cancer
- Coronary heart disease
- Stroke

- Venous thromboembolism (deep vein thrombosis and pulmonary embolism)
- Cognition and dementia
- Endometrial and ovarian cancer
- Cholecystitis

GUIDELINE CATEGORY

Prevention

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To summarize the U.S. Preventive Services Task Force (USPSTF) recommendations on hormone therapy for the prevention of chronic conditions in postmenopausal women and the supporting scientific evidence
- To update the USPSTF 2002 recommendations on hormone replacement therapy

TARGET POPULATION

Postmenopausal women

INTERVENTIONS AND PRACTICES CONSIDERED

Hormone replacement therapy (HRT)

- Combined estrogen and progestin (considered, but not recommended)
- Unopposed estrogen (considered, but not recommended)

MAJOR OUTCOMES CONSIDERED

The use of postmenopausal hormone replacement therapy (HRT) and:

- Coronary heart disease and stroke incidence and/or mortality

- Risk of venous thromboembolism, including deep venous thrombosis (DVT), pulmonary embolism, or both
- Bone mineral density (BMD) and risk of fracture
- Cognitive function, including verbal memory, vigilance, reasoning, and motor speed
- Breast cancer incidence, mortality, or both
- Colon, endometrial, and ovarian cancer incidence and/or mortality
- Risk of cholecystitis and rate of biliary tract surgery

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The U.S. Preventive Services Task Force (USPSTF) grades the quality of the overall evidence on a 3-point scale (good, fair, or poor).

Good

Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

Fair

Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies; generalizability to routine practice; or indirect nature of evidence on health outcomes.

Poor

Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct,

gaps in the chain of evidence, or lack of information on important health outcomes.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Balance Sheets
Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

When the overall quality of the evidence is judged to be good or fair, the U.S. Preventive Services Task Force (USPSTF) proceeds to consider the magnitude of net benefit to be expected from implementation of the preventive service. Determining net benefit requires assessing both the magnitude of benefits and the magnitude of harms and weighing the two.

The USPSTF classifies benefits, harms, and net benefits on a 4-point scale: "substantial," "moderate," "small," and "zero/negative."

"Outcomes tables" (similar to 'balance sheets') are the USPSTF's standard resource for estimating the magnitude of benefit. These tables, prepared by the topic teams for use at USPSTF meetings, compare the condition specific outcomes expected for a hypothetical primary care population with and without use of the preventive service. These comparisons may be extended to consider only people of specified age or risk groups or other aspects of implementation. Thus, outcomes tables allow the USPSTF to examine directly how the preventive services affect benefits for various groups.

When evidence on harms is available, the topic teams assess its quality in a manner like that for benefits and include adverse events in the outcomes tables. When few harms data are available, the USPSTF does not assume that harms are small or nonexistent. It recognizes a responsibility to consider which harms are likely and judge their potential frequency and the severity that might ensue from implementing the service. It uses whatever evidence exists to construct a general confidence interval on the 4-point scale (e.g., substantial, moderate, small, and zero/negative).

Value judgments are involved in using the information in an outcomes table to rate either benefits or harms on the USPSTF's 4-point scale. Value judgments are also needed to weigh benefits against harms to arrive a rating of net benefit.

In making its determinations of net benefit, the USPSTF strives to consider what it believes are the general values of most people. It does this with greater confidence for certain outcomes (e.g., death) about which there is little disagreement about undesirability, but it recognizes that the degree of risk people are willing to accept to avert other outcomes (e.g., cataracts) can vary considerably. When the USPSTF perceives that preferences among individuals vary greatly, and that these variations are sufficient to make trade-off of benefits and harms a "close-call," then it will often assign a C recommendation (see the "Recommendation Rating Scheme" field). This recommendation indicates the decision is likely to be sensitive to individual patient preferences.

The USPSTF uses its assessment of the evidence and magnitude of net benefit to make recommendations. The general principles the USPSTF follows in making recommendations are outlined in Table 5 of the companion document cited below. The USPSTF liaisons on the topic team compose the first drafts of the recommendations and rationale statements, which the full panel then reviews and edits. Recommendations are based on formal voting procedures that include explicit rules for determining the views of the majority.

From: Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow, CD, Teutsch SM, Atkins D. Current methods of the U.S. Preventive Services Task Force: a review of the process. Methods Work Group, Third U.S. Preventive Services Task Force. Am J Prev Med 2001 Apr;20(3S):21-35.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The U.S. Preventive Services Task Force (USPSTF) grades its recommendations according to one of five classifications (A, B, C, D, or I), reflecting the strength of evidence and magnitude of net benefit (benefits minus harms).

A

The U.S. Preventive Services Task Force (USPSTF) strongly recommends that clinicians provide [the service] to eligible patients. The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.

B

The U.S. Preventive Services Task Force (USPSTF) recommends that clinicians provide [the service] to eligible patients. The USPSTF found at least fair evidence that [the service] improves health outcomes and concludes that benefits outweigh harms.

C

The U.S. Preventive Services Task Force (USPSTF) makes no recommendation for or against routine provision of [the service]. The USPSTF found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms it too close to justify a general recommendation.

D

The U.S. Preventive Services Task Force (USPSTF) recommends against routinely providing [the service] to asymptomatic patients. The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.

I

The U.S. Preventive Services Task Force (USPSTF) concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. Evidence that [the service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Comparison with Guidelines from Other Groups
External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Peer Review. Before the U.S. Preventive Services Task Force makes its final determinations about recommendations on a given preventive service, the Evidence-based Practice Center and the Agency for Healthcare Research and Quality send a draft systematic evidence review to 4 to 6 external experts and to federal agencies and professional and disease-based health organizations with interests in the topic. They ask the experts to examine the review critically for accuracy and completeness and to respond to a series of specific questions about the document. After assembling these external review comments and documenting the proposed response to key comments, the topic team presents this information to the Task Force in memo form. In this way, the Task Force can consider these external comments and a final version of the systematic review before it votes on its recommendations about the service. Draft recommendations are then circulated for comment from reviewers representing professional societies, voluntary organizations, and Federal agencies. These comments are discussed before the whole U.S. Preventive Services Task Force before final recommendations are confirmed.

Recommendations of Others. Recommendations regarding the use of hormone therapy for the prevention of chronic diseases in postmenopausal women from the following groups were discussed: the American College of Obstetricians and Gynecologists (ACOG), the American Heart Association (AHA), the Canadian Task Force on Preventive Health Care (CTFPHC), and the North American Menopause Society (NAMS).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The U.S. Preventive Services Task Force (USPSTF) grades its recommendations (A, B, C, D, or I) and the quality of the overall evidence for a service (good, fair, poor). The definitions of these grades can be found at the end of the "Major Recommendations" field.

The USPSTF recommends against the routine use of combined estrogen and progestin for the prevention of chronic conditions in postmenopausal women. D recommendation

The USPSTF found good evidence that the use of combined estrogen and progestin results in both benefits and harms. Benefits include reduced risk for fracture (good evidence) and colorectal cancer (fair evidence). Combined estrogen and progestin has no beneficial effect on coronary heart disease and may even pose an increased risk (good evidence). Other harms include increased risk for breast cancer (good evidence), venous thromboembolism (good evidence), stroke (fair evidence), cholecystitis (fair evidence), dementia (fair evidence), and lower global cognitive function (fair evidence).

Because of insufficient evidence, the USPSTF could not assess the effects of combined estrogen and progestin on the incidence of ovarian cancer, mortality from breast cancer or coronary heart disease, or all-cause mortality. The USPSTF concluded that the harmful effects of combined estrogen and progestin are likely to exceed the chronic disease prevention benefits in most women.

The USPSTF recommends against the routine use of unopposed estrogen for the prevention of chronic conditions in postmenopausal women who have had a hysterectomy. D recommendation

The USPSTF found good evidence that the use of unopposed estrogen results in both benefits and harms. The benefits include reduced risk for fracture (good evidence). Harms include increased risk for venous thromboembolism (fair evidence), stroke (fair evidence), dementia (fair evidence), and lower global cognitive functioning (fair evidence). There is fair evidence that unopposed estrogen has no beneficial effect on coronary heart disease.

Because of insufficient evidence, the USPSTF could not assess the effects of unopposed estrogen on the incidence of breast cancer, ovarian cancer, or colorectal cancer as well as breast cancer mortality or all-cause mortality. The USPSTF concluded that the harmful effects of unopposed estrogen are likely to exceed the chronic disease prevention benefits in most women.

Clinical Considerations

- The balance of benefits and harms for a woman will be influenced by her personal preferences, her risks for specific chronic diseases, and the presence of menopausal symptoms. A shared decision-making approach to preventing chronic diseases in perimenopausal and postmenopausal women involves

consideration of individual risk factors and preferences in selecting effective interventions for reducing the risks for fracture, heart disease, and cancer. Other USPSTF recommendations for prevention of chronic diseases (screening for osteoporosis, high blood pressure, lipid disorders, breast cancer, and colorectal cancer; and counseling to prevent tobacco use) are available at www.preventiveservices.ahrq.gov.

- The USPSTF did not consider the use of hormone therapy for the management of menopausal symptoms, which is the subject of recommendations by other expert groups. Women and their clinicians should discuss the balance of risks and benefits before deciding to initiate or continue hormone therapy for menopausal symptoms. For example, for combined estrogen and progestin, some risks (such as the risks for venous thromboembolism, coronary heart disease [CHD], and stroke) arise within the first 1 to 2 years of therapy, and other risks (such as the risk for breast cancer) appear to increase with longer-term hormone therapy. The populations of women using hormone therapy for symptom relief may differ from those who would use hormone therapy for prevention of chronic disease (e.g., age differences). Other expert groups have recommended that women who decide to take hormone therapy to relieve menopausal symptoms use the lowest effective dose for the shortest possible time.
- Although estrogen alone or in combination with progestin reduces the risk for fractures in women, other effective medications (e.g., bisphosphonates and calcitonin) are available for treating women with low bone density to prevent fractures. The role of chemopreventive agents in preventing fractures in women without low bone density is unclear. The USPSTF addressed screening for osteoporosis in postmenopausal women in 2002.
- Unopposed estrogen increases the risk for endometrial cancer in women who have an intact uterus. Clinicians should use a shared decision-making approach when discussing the possibility of using unopposed estrogen in women who have not had a hysterectomy.

Definitions:

Strength of Recommendations

The U.S. Preventive Services Task Force (USPSTF) grades its recommendations according to one of five classifications (A, B, C, D, or I), reflecting the strength of evidence and magnitude of net benefit (benefits minus harms).

A

The U.S. Preventive Services Task Force (USPSTF) strongly recommends that clinicians provide [the service] to eligible patients. The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.

B

The U.S. Preventive Services Task Force (USPSTF) recommends that clinicians provide [the service] to eligible patients. The USPSTF found at least fair evidence that [the service] improves health outcomes and concludes that benefits outweigh harms.

C

The U.S. Preventive Services Task Force (USPSTF) makes no recommendation for or against routine provision of [the service]. The US Preventive Services Task Force found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms it too close to justify a general recommendation.

D

The U.S. Preventive Services Task Force (USPSTF) recommends against routinely providing [the service] to asymptomatic patients. The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.

I

The U.S. Preventive Services Task Force (USPSTF) concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. Evidence that [the service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.

Strength of Evidence

The U.S. Preventive Services Task Force (USPSTF) grades the quality of the overall evidence for a service on a 3-point scale (good, fair, or poor).

Good

Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

Fair

Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies; generalizability to routine practice; or indirect nature of evidence on health outcomes.

Poor

Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The updated statement is based on the results of the Women's Health Initiative randomized controlled trial as well as the information in the 2002 summary of the evidence on this topic. The type of evidence supporting each recommendation is identified in the "Major Recommendations" field.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Osteoporosis and Fractures

Good evidence from observational studies and randomized clinical trials demonstrates that estrogen therapy increases bone density and reduces the risk for fractures. The combined estrogen-progestin arm of the Women's Health Initiative (WHI) trial, a fair-quality study, found significant reductions in total fracture risk (hazard ratio [HR], 0.76; adjusted 95% confidence interval [CI], 0.63-0.92) among healthy women taking estrogen and progestin. This arm of the WHI trial also showed reductions for hip and vertebral fracture, although these did not achieve statistical significance. (In its analysis, the USPSTF used nominal 95% CIs for the primary outcomes and adjusted 95% CIs for all secondary outcomes.)

The estrogen-only arm of the WHI trial also reported decreased risk for hip and vertebral fracture, which also did not reach statistical significance. A meta-analysis of 22 trials of estrogen reported an overall 27% reduction in non-vertebral fractures (relative risk [RR], 0.73; [95% CI, 0.56-0.94]), although the quality of individual studies varied. The Heart and Estrogen/progestin Replacement Study (HERS) and its unblinded follow-up study, HERS II, a fair-quality trial of combined estrogen-progestin for the secondary prevention of heart disease that reported many other outcomes, found no reduction in hip, wrist, vertebral, or total fractures with hormone therapy (relative hazard [RH] for total fractures, 1.04; 95% CI, 0.87-1.25). Overall, a good-quality body of evidence supports the efficacy of hormone therapy in increasing bone density and decreasing fracture risk.

Colorectal Cancer

Results from the WHI study and HERS showed a trend toward reduced incidence of colon cancer (HR, 0.63; adjusted 95% CI, 0.32-1.24 and RH, 0.81; 95% CI, 0.46-1.45, respectively), but the trend did not reach statistical significance. The estrogen-only arm of the WHI trial showed neither benefit nor harm for colorectal cancer risk (HR, 1.08; adjusted 95% CI, 0.63-1.86). A meta-analysis of 18 observational studies of postmenopausal women reported a 20% reduction in colon cancer (RR, 0.80; 95% CI, 0.74-0.86) and a 19% reduction in rectal cancer (RR, 0.81; 95% CI, 0.72-0.92) among women who had ever used combined estrogen-progestin or estrogen alone compared with women who had never used hormone therapy. This decrease in risk was more apparent when current users were compared with those who had never used hormone therapy (RR, 0.66; 95%

CI, 0.59-0.74). Overall, the evidence suggesting a trend toward reduction of colorectal cancer risk with combined hormone therapy should be interpreted cautiously until controlled trials clarify whether therapy has either no benefit or modest benefit.

POTENTIAL HARMS

Breast Cancer

The estrogen-progestin arm of the Women's Health Initiative (WHI) study was terminated after an average of 5.2 years of follow-up because "evidence for breast cancer harm, along with evidence for some increase in coronary heart disease (CHD), stroke, and pulmonary embolism, outweighed the evidence of benefit for fractures and possible benefit for colon cancer." This study showed an increased invasive breast cancer incidence (hazard ratio [HR], 1.26; nominal 95% confidence interval [CI], 1.00-1.59). However, no effect on breast cancer mortality was observed. Comparable increases in breast cancer incidence were observed among women taking estrogen and progestin over 6.8 years of follow-up in the Heart and Estrogen/progestin Replacement Study (HERS). The U.K. Million Women Study, a fair-quality study, showed an increased risk for breast cancer in current users of combined estrogen-progestin (relative risk [RR], 2.00; 95% CI, 1.91-2.09) compared with those who had never used hormone therapy. Results from two good-quality cohort studies conflict on the effects of long-term hormone therapy on breast cancer mortality. Overall, there is a good-quality body of evidence indicating that combined estrogen-progestin increases breast cancer risk. It is unclear whether the combination of estrogen-progestin confers a greater breast cancer risk than estrogen alone. In studies of estrogen alone, the results are conflicting: the Million Women Study showed an increased risk for breast cancer in current users of estrogen only (RR, 1.30; 95% CI, 1.22-1.38) compared with those who had never used it; but the estrogen-only arm of the WHI trial showed a trend toward breast cancer prevention (HR, 0.77; nominal 95% CI, 0.59-1.01).

Coronary Heart Disease (CHD)

In the WHI study, women who took combined estrogen-progestin daily, compared with women taking placebo, had an increased risk for CHD (fatal and non-fatal myocardial infarctions), which became evident shortly after initiation of the study (HR, 1.29; nominal 95% CI, 1.02-1.63). However, mortality from CHD was not significantly increased among the women taking combined hormone therapy daily. One meta-analysis of observational studies showed a statistically significant reduction in CHD (RR, 0.80; 95% CI, 0.68-0.95) among current hormone therapy users, but not among those who had used hormone therapy in the past or among those who had never used it. This meta-analysis also showed that CHD mortality in observational studies was reduced among current hormone therapy users (RR, 0.62; 95% CI, 0.40-0.90) but was not reduced among those who had used hormone therapy in the past. However, among studies that controlled for socioeconomic status (social class, education, or income), no CHD benefit was seen among current hormone therapy users, suggesting that the observed difference may be due to confounding by socioeconomic status and other lifestyle factors (e.g., exercise or alcohol use) rather than use of hormone therapy. Thus, selection bias (in this case, the tendency of healthier women to use hormone

therapy) appears to explain the apparent protective effect of estrogen against CHD seen in observational studies. The estrogen-only arm of the WHI trial showed no decreased risk for CHD.

Stroke

A meta-analysis of 9 observational primary prevention studies suggests that hormone therapy is associated with a small increase in stroke incidence (RR, 1.12; 95% CI, 1.01-1.23), due primarily to an increase in thromboembolic stroke (RR, 1.20; 95% CI, 1.01-1.40). The risk for subarachnoid bleeding and hemorrhagic stroke was not increased, and the overall stroke mortality was marginally reduced (RR, 0.81; 95% CI, 0.71-0.92). These results are consistent with findings from the WHI, which reported increased incidence of stroke in women taking combined estrogen-progestin daily (HR, 1.41; adjusted 95% CI, 0.86-2.31). The estrogen-only arm of the WHI trial, which was terminated after an average of 6.8 years of follow-up, showed a trend toward increased stroke risk with unopposed estrogen use (HR, 1.39; adjusted 95% CI, 0.97-1.99).

Venous Thromboembolism (Deep Venous Thrombosis and Pulmonary Embolism)

In a meta-analysis of 12 studies (3 randomized controlled trials, 8 case-control studies, and 1 cohort study), hormone therapy (estrogen alone or in combination with progestin) was associated with an increased risk for venous thromboembolism (RR, 2.14; 95% CI, 1.64-2.81). Five of 6 studies that examined the effects of hormone therapy over time reported that the risk was highest within the first year of use (RR, 3.49; 95% CI, 2.33-5.59). These results are consistent with the findings in the estrogen-progestin arm of the WHI, which reported a 2-fold increased rate of venous thromboembolic disease, including deep venous thrombosis and pulmonary embolism, in women taking combined estrogen-progestin daily. The estrogen-only arm of the WHI trial showed a trend toward increased risk for venous thromboembolism with unopposed estrogen use (HR, 1.33; adjusted 95% CI, 0.86-2.08).

Cognition and Dementia

While earlier studies showed a beneficial effect of hormone therapy on cognition, these studies had marked heterogeneity and variation in assessment of outcomes. For example, 9 randomized controlled trials examining the effect of hormone therapy on cognition in women showed improvement in verbal memory, vigilance, reasoning, and motor speed; however, these trials may have biased results, since they were conducted with women experiencing menopausal symptoms at baseline. A meta-analysis of 12 observational studies (1 of good quality, 3 of fair quality, and 8 of poor quality) showed a reduction in the risk for dementia among postmenopausal women taking hormone therapy (RR, 0.66; 95% CI, 0.53-0.82). Because of issues of internal and external validity from these previous studies, the more recent, fair-quality WHI memory studies are more likely to represent the effects of hormone therapy use in the healthy postmenopausal population. The WHI memory study showed decreased global cognitive function (measured by the modified Mini-Mental State Examination) in women taking estrogen alone and in the pooled group of women taking estrogen alone or estrogen-progestin. The WHI memory study also showed an increased risk for probable dementia or mild

cognitive impairment in both the estrogen-alone (HR, 1.38; 95% CI, 1.01-1.89) and estrogen-progestin (HR, 1.44; 95% CI, 1.04-1.99) arms of the trial. The overall evidence supports harmful effects of hormone therapy on cognitive function, although the clinical relevance of this difference in cognitive function is unclear.

Endometrial and Ovarian Cancer

Results of a meta-analysis of 29 good-quality observational studies of endometrial cancer reported a relative risk of 2.3 for users of unopposed estrogen compared with nonusers. Risks increased with increasing duration of use (RR, 9.5 for 10 years of use), and the risk for endometrial cancer remained elevated 5 or more years after discontinuation of unopposed estrogen therapy. Estrogen and progestin did not increase the risk for endometrial cancer in HERS or in the WHI.

Data on the association between the use of hormone therapy and the risk for ovarian cancer are inconsistent. Two good-quality cohort studies reported increased risks for ovarian cancer or ovarian cancer mortality among women who had taken hormone therapy for 10 years or more. However, a third study found no effect of hormone therapy on ovarian cancer mortality. One study suggested higher risk with unopposed estrogen than with estrogen-progestin therapy, but data are insufficient to resolve the effects of different formulations or doses of hormone therapy on ovarian cancer risk. Neither the WHI nor HERS reported risk for ovarian cancer.

Cholecystitis

Results from the Nurses' Health Study, a good-quality cohort study, reported an increased risk for cholecystitis among current hormone therapy users and long-term users (>5 years) compared with nonusers. Risk for cholecystitis remained elevated among past users. An increase in biliary tract surgery during 6.8 years of follow-up was reported among women taking estrogen plus progestin compared with those taking placebo in HERS. The WHI has not reported on outcomes for biliary tract disease among women taking hormone therapy.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Recommendations made by the U.S. Preventive Services Task Force (USPSTF) are independent of the U.S. Government. They should not be construed as an official position of the Agency for Healthcare Research and Quality (AHRQ) or the U.S. Department of Health and Human Services.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The experiences of the first and second U.S. Preventive Services Task Force (USPSTF), as well as that of other evidence-based guideline efforts, have

highlighted the importance of identifying effective ways to implement clinical recommendations. Practice guidelines are relatively weak tools for changing clinical practice when used in isolation. To effect change, guidelines must be coupled with strategies to improve their acceptance and feasibility. Such strategies include enlisting the support of local opinion leaders, using reminder systems for clinicians and patients, adopting standing orders, and audit and feedback of information to clinicians about their compliance with recommended practice.

In the case of preventive services guidelines, implementation needs to go beyond traditional dissemination and promotion efforts to recognize the added patient and clinician barriers that affect preventive care. These include clinicians' ambivalence about whether preventive medicine is part of their job, the psychological and practical challenges that patients face in changing behaviors, lack of access to health care or of insurance coverage for preventive services for some patients, competing pressures within the context of shorter office visits, and the lack of organized systems in most practices to ensure the delivery of recommended preventive care.

Dissemination strategies have changed dramatically in this age of electronic information. While recognizing the continuing value of journals and other print formats for dissemination, the Agency for Healthcare Research and Quality will make all U.S. Preventive Services Task Force (USPSTF) products available through its Web site. The combination of electronic access and extensive material in the public domain should make it easier for a broad audience of users to access U.S. Preventive Services Task Force materials and adapt them for their local needs. Online access to U.S. Preventive Services Task Force products also opens up new possibilities for the appearance of the annual, pocket-size Guide to Clinical Preventive Services.

To be successful, approaches for implementing prevention have to be tailored to the local level and deal with the specific barriers at a given site, typically requiring the redesign of systems of care. Such a systems approach to prevention has had notable success in established staff-model health maintenance organizations, by addressing organization of care, emphasizing a philosophy of prevention, and altering the training and incentives for clinicians. Staff-model plans also benefit from integrated information systems that can track the use of needed services and generate automatic reminders aimed at patients and clinicians, some of the most consistently successful interventions. Information systems remain a major challenge for individual clinicians' offices, however, as well as for looser affiliations of practices in network-model managed care and independent practice associations, where data on patient visits, referrals, and test results are not always centralized.

IMPLEMENTATION TOOLS

Foreign Language Translations
Patient Resources
Personal Digital Assistant (PDA) Downloads
Pocket Guide/Reference Cards
Tool Kits

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

RELATED QUALITY TOOLS

- A Step-by-Step Guide to Delivering Clinical Preventive Services: A Systems Approach

- Postmenopausal Hormone Replacement Therapy for Primary Prevention of Chronic Conditions. What's New from the USPSTF.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

U.S. Preventive Services Task Force. Hormone therapy for the prevention of chronic conditions in postmenopausal women: recommendations from the U.S. Preventive Services Task Force. Ann Intern Med 2005 May 17;142(10):855-60. [30 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1996 (revised 2005 May 17)

GUIDELINE DEVELOPER(S)

United States Preventive Services Task Force - Independent Expert Panel

GUIDELINE DEVELOPER COMMENT

The U.S. Preventive Services Task Force (USPSTF) is a Federally-appointed panel of independent experts. Conclusions of the USPSTF do not necessarily reflect policy of the U.S. Department of Health and Human Services (DHHS) or DHHS agencies.

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

U.S. Preventive Services Task Force (USPSTF)

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Corresponding Author: Ned Calonge, MD, MPH, Chair, U.S. Preventive Services Task Force (USPSTF), c/o Program Director, USPSTF, Agency for Healthcare Research and Quality

Task Force Members*: Ned Calonge, MD, MPH, Chair, USPSTF (Acting Chief Medical Officer and State Epidemiologist, Colorado Department of Public Health and Environment, Denver, CO); Janet D. Allan, PhD, RN, CS, Vice-chair, USPSTF (Dean, School of Nursing, University of Maryland Baltimore, Baltimore, MD); Alfred O. Berg, MD, MPH, (Professor and Chair, Department of Family Medicine, University of Washington, Seattle, WA); Paul S. Frame, MD (Tri-County Family Medicine, Cohocton, NY, and Clinical Professor of Family Medicine, University of Rochester, Rochester, NY); Leon Gordis, MD, MPH, DrPH (Professor, Epidemiology Department, Johns Hopkins Bloomberg School of Public Health, Baltimore MD); Kimberly D. Gregory, MD, MPH (Director, Women's Health Services Research and Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Cedars-Sinai Medical Center, Los Angeles, CA); Russell Harris, MD, MPH (Associate Professor of Medicine, Sheps Center for Health Services Research, University of North Carolina School of Medicine, Chapel Hill, NC); Mark S. Johnson, MD, MPH (Professor and Chair, Department of Family Medicine, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, NJ); Jonathan D. Klein, MD, MPH (Associate Professor, Department of Pediatrics, University of Rochester School of Medicine, Rochester, NY); Carol Loveland-Cherry, PhD, RN (Executive Associate Dean, Office of Academic Affairs, University of Michigan School of Nursing, Ann Arbor, MI); Virginia A. Moyer, MD, MPH (Professor, Department of Pediatrics, University of Texas Health Sciences Center, Houston, TX); Judith K. Ockene, PhD (Professor of Medicine and Chief of Division of Preventive and Behavioral Medicine, University of Massachusetts Medical School, Worcester, MA); Diana B. Petitti, MD, MPH (Senior Scientific Advisor for Health Policy and Medicine, Regional Administration, Kaiser Permanente Southern California, Pasadena, CA); Albert L. Siu, MD, MSPH (Professor and Chairman, Brookdale Department of Geriatrics and Adult Development, Mount Sinai Medical Center, New York, NY); Steven M. Teutsch, MD, MPH (Executive Director, Outcomes Research and Management, Merck & Company, Inc., West Point, PA); and Barbara P. Yawn, MD, MSc (Director of Research, Olmstead Research Center, Rochester, MN).

*Members of the USPSTF at the time this recommendation was finalized. For a list of current Task Force members, go to www.ahrq.gov/clinic/uspstfab.htm.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The U.S. Preventive Services Task force has an explicit policy concerning conflict of interest. All members and evidence-based practice center (EPC) staff disclose at each meeting if they have an important financial conflict for each topic being discussed. Task Force members and EPC staff with conflicts can participate in discussions about evidence, but members abstain from voting on recommendations about the topic in question.

Steven M. Teutsch, MD, MPH, recused himself from voting on this topic.

From: Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow, CD, Teutsch SM, Atkins D. Current methods of the U.S. Preventive Services Task Force: a review of the process. Methods Work Group, Third U.S. Preventive Services Task Force. Am J Prev Med 2001 Apr;20(3S):21-35.

GUIDELINE STATUS

This is the current release of the guideline.

This release updates a previously published guideline: Postmenopausal hormone replacement therapy for primary prevention of chronic conditions: recommendations and rationale. Ann Intern Med 2002 Nov 19;137(10):834-9.

GUIDELINE AVAILABILITY

Electronic copies: Available from the U.S. Preventive Services Task Force (USPSTF) Web site. Also available from the Annals of Internal Medicine Online.

Print copies: Available from the Agency for Healthcare Research and Quality (AHRQ) Publications Clearinghouse. For more information, go to http://www.ahrq.gov/news/pubsix.htm or call 1-800-358-9295 (U.S. only).

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

Evidence Reviews:

- Nelson H, Humphrey L, LeBlanc E, et al. Postmenopausal hormone replacement therapy for the primary prevention of chronic conditions: a summary of the evidence. Rockville (MD); Agency for Healthcare Research and Quality; 2002 Aug. Electronic copies available from the Agency for Healthcare Research and Quality (AHRQ) Web site.
- Humphrey LL, Takano L, and Chan BKS. Postmenopausal hormone replacement therapy and cardiovascular disease. Rockville (MD); Agency for Healthcare Research and Quality; 2002 Sep. (Systematic evidence review; no. 10). Electronic copies available from the AHRQ Web site.
- Miller J, Chan BKS, Nelson HD. Hormone replacement therapy and risk of venous thromboembolism. Rockville (MD); Agency for Healthcare Research and Quality; 2002 Aug. (Systematic evidence review; no. 11). Electronic

copies available from the AHRQ Web site. Also available from the National Library of Medicine Health Services/Technology Assessment Text (HSTAT) database.
- Nelson HD. Hormone replacement therapy and osteoporosis. Rockville (MD); Agency for Healthcare Research and Quality; 2002 Aug. (Systematic evidence review; no. 12). Electronic copies available from the AHRQ Web site.
- LeBlanc E, Chan B, Nelson H. Hormone replacement therapy and cognition. Rockville (MD); Agency for Healthcare Research and Quality; 2002 Aug. (Systematic evidence review; no. 13). Electronic copies available from the AHRQ Web site.
- Humphrey LL, Chan BKS. Hormone replacement therapy and breast cancer. Rockville (MD); Agency for Healthcare Research and Quality; 2002 Aug. (Systematic evidence review; no. 14). Electronic copies available from the AHRQ Web site.
- Humphrey LL, Chan BK, Sox HC. Postmenopausal hormone replacement therapy and the primary prevention of cardiovascular disease. Ann Intern Med. 2002 Aug 20;137(4):273-84. Electronic copies available from the Annals of Internal Medicine Online.
- Miller J, Chan BK, Nelson HD. Postmenopausal estrogen replacement and risk for venous thromboembolism: a systematic review and meta-analysis for the U.S. Preventive Services Task Force. Ann Intern Med. 2002 May 7;136(9):680-90. Electronic copies available from the Annals of Internal Medicine Online.
- LeBlanc E, Janowsky J, Chan B, Nelson H. Hormone replacement therapy and cognition: systematic review and meta-analysis. JAMA 2001 Mar 21;285(11):1489-99.
- Nelson H, Humphrey L, Nygren P, Teutsch S, Allan J. Postmenopausal hormone replacement therapy: scientific review. JAMA 2002 Aug 21;288(7):872-81.

Background Articles:

- Woolf SH, Atkins D. The evolving role of prevention in health care: contributions of the U.S. Preventive Services Task Force. Am J Prev Med 2001 Apr;20(3S):13-20.
- Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow, CD, Teutsch SM, Atkins D. Current methods of the U.S. Preventive Services Task Force: a review of the process. Methods Work Group, Third U.S. Preventive Services Task Force. Am J Prev Med 2001 Apr;20(3S):21-35.
- Saha S, Hoerger TJ, Pignone MP, Teutsch SM, Helfand M, Mandelblatt. The art and science of incorporating cost effectiveness into evidence-based recommendations for clinical preventive services. Cost Work Group of the Third U.S. Preventive Services Task Force. Am J Prev Med 2001 Apr;20(3S):36-43.

Electronic copies: Available from U.S. Preventive Services Task Force (USPSTF) Web site.

The following are also available:

- The guide to clinical preventive services, 2005. Recommendations of the U.S. Preventive Services Task Force. Rockville (MD): Agency for Healthcare

Research and Quality (AHRQ), 2005. 192 p. Electronic copies available from the AHRQ Web site.

Print copies: Available from the Agency for Healthcare Research and Quality Publications Clearinghouse. For more information, go to http://www.ahrq.gov/news/pubsix.htm or call 1-800-358-9295 (U.S. only).

The Interactive Preventive Services Selector tool, which enables users to search USPSTF recommendations by patient age, sex, and pregnancy status, is available as a web-based version or PDA application. It is available from the AHRQ Web site.

PATIENT RESOURCES

The following is available:

- The Pocket Guide to Good Health for Adults. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 2003.

  Electronic copies: Available from the U.S. Preventive Services Task Force (USPSTF) Web site. Copies also available in Spanish from the USPSTF Web site.

  Print copies: Available from the Agency for Healthcare Research and Quality (AHRQ) Publications Clearinghouse. For more information, go to http://www.ahrq.gov/news/pubsix.htm or call 1-800-358-9295 (U.S. only).

- Summaries for patients. Hormone therapy to prevent chronic conditions in postmenopausal women: recommendations from the U.S. Preventive Services Task Force. Ann Intern Med 2005 May 17; 142(10):I-59.

  Electronic copies: Available from the Annals of Internal Medicine Online.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This summary was completed by ECRI on June 30, 1998. The information was verified by the guideline developer on December 1, 1998. This summary was updated on October 11, 2002. The information was verified by the guideline developer on October 11, 2002. This summary was updated by ECRI on May 3, 2005. The information was verified by the guideline developer on May 9, 2005.

COPYRIGHT STATEMENT

Requests regarding copyright should be sent to: Gerri M. Dyer, Electronic Dissemination Advisor, Agency for Healthcare Research and Quality (formerly the Agency for Health Care Policy and Research), Center for Health Information Dissemination, Suite 501, Executive Office Center, 2101 East Jefferson Street, Rockville, MD 20852; Facsimile: 301-594-2286; E-mail: gdyer@ahrq.gov.

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx.

NGC, AHRQ, and its contractor ECRI make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 9/25/2006